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Subject Index

24. Oral Fluid Validity Testing

1. Subject: Role of the Certifying Technician (CT)

Discussion: Currently, laboratories may designate "negative certifying scientists" to certify negative initial drug test results and normal or dilute specimen validity test results. The "Certifying Technician" will replace the negative certifying scientist and these individuals will be key staff at laboratories and IITFs. The revised Guidelines should more clearly describe the role of the CT, including the types of specimens that a CT can certify (i.e., "negative" and "negative, dilute" results). A CT must also be allowed to certify specimens as rejected for testing. Because an IITF is not allowed to report specimens as invalid and is required to send all "invalid" specimens to a certified laboratory, references in the proposed Guidelines to "invalid result" reports from IITFs should be deleted.

2. Subject: Specimens Rejected for Testing

Discussion: The Guidelines should provide necessary guidance/instructions on dealing with specimens rejected for testing.

Issue 1: The revised Guidelines do not describe specimen disposition and actions to be taken after a specimen is reported as rejected for testing by a testing facility (i.e., laboratory, POCT tester, or IITF).

Issue 2: The revised Guidelines do not address specimen rejection at a POCT site or IITF. A POCT tester must use Guidelines criteria for specimen evaluation prior to testing, the same as used by an IITF or laboratory (Sections 16.1 and 16.2). Therefore, the POCT tester must be allowed to reject specimens that fail to meet the criteria. The Guidelines should also appropriately address specimen rejection at an IITF (see recommended revisions in Subject 1 above).

3. Subject 6-Acetylmorphine (6-AM) Testing

Discussion: Under the current Guidelines, certified urine laboratories are required to

perform an opiates initial test, perform opiates confirmatory testing based on the initial test results, and then perform confirmatory testing for 6-acetylmorphine when a specimen's morphine result is at or above 2000 ng/mL.

The revised Guidelines allow the option to perform an initial test for 6-AM (i.e., all specimen types). The revised Guidelines further state, for urine specimens, "If a laboratory uses both initial test kits to screen a specimen concurrently, it may report 6-AM alone." Additional guidance should be provided to prevent inconsistent treatment of specimens. Testing facilities that choose to use both opiates and 6-AM initial tests concurrently may report specimens as positive for 6-AM based on 6-AM initial and confirmatory tests, without regard to the quantitative morphine result. Those testing facilities performing only the opiates initial test would not perform 6-AM testing unless the morphine confirmatory test result was at or above 2000 ng/mL.

Issue 1: If a specimen is presumptive positive on both the opiates and 6-AM initial tests, and the laboratory performs opiates and 6-AM confirmatory tests, **how is the specimen reported when 6-AM is positive and the quantitative morphine result is negative (i.e., <2000 ng/mL)?**

a) HHS could continue to require 6-AM testing on all specimens **with a positive morphine result in the confirmatory test**. But the Guidelines could allow laboratories to perform a 6-AM initial test (with the same cutoff as the confirmatory 6-AM test) on morphine-positive specimens and reflex only presumptive positive 6-AM specimens to a confirmatory test.

OR

b) HHS could remove the requirement for an associated positive morphine result (i.e., test and report 6-AM regardless of the morphine result) and **require** laboratories and IITFs to perform a 6-AM initial test in addition to an opiates initial test. Any specimen with a positive 6-AM initial test result would be reflexed for 6-AM confirmatory testing, regardless of the opiates initial or confirmatory test

results.

We believe that there is justification for either option. There is mounting evidence that 6-AM positive specimens are not being reported due to the requirement for a morphine positive result. Option b would address this issue. It should be noted that, under option b, POCT testing for 6-AM should also be required for consistency.

Issue 2: The Guidelines state that the 6-AM initial test is permitted. It is unclear whether the test will be required in addition to, simultaneously with, or in lieu of, an opiates initial test.

Issue 3: Requirements should be consistent for all specimen matrices.

4. Subject: Establishing Testing Cutoffs for Alternate Matrices

Discussion: Cutoffs utilized by the Federal Government in its workplace drug testing programs must meet scientific and forensic scrutiny. The process employed by HHS in establishing testing cutoffs has been based on evaluation of the scientific literature to determine concentrations that are relevant to the intended use, recommendations of the industries that will be required to adhere to the cutoffs and evaluation of the capabilities of the testing technology with pilot performance testing (PT) programs.

HHS has conducted pilot PT programs for the alternate specimen matrices through the National Laboratory Certification Program (NLCP) since April 2000. These pilot PT programs have provided essential information for evaluating the capabilities of the technologies utilized in the testing of new specimen matrices as well as the ability of the industries employing these technologies to meet proposed cutoffs. The data obtained from the pilot PT programs have resulted in numerous revisions to proposed cutoffs as performance capabilities were realized. One final adjustment to the cutoffs proposed by HHS is suggested in the subject below concerning hair testing.

5. Subject: Hair Testing

Discussion: The Guidelines section on hair testing should be based on practical knowledge of hair test collection and testing procedures, to ensure effective testing for drugs in hair and appropriate measures for assessing hair specimen validity.

Issue 1: Based on results of the NLCP Pilot PT program for hair, laboratories may not be able to confirm at 40% of the proposed cutoff. The confirmation cutoff for THCA should be 0.1 pg/mg and not 0.05 pg/mg.

Issue 2: A "digestion test" is listed, but is not defined and it is unclear what information would be obtained from such a test.

Issue 3: It would not be useful for a testing facility to use microscopic examination to detect substitution (i.e., synthetic hair). Hair collection is an "observed collection" with the donor not touching the specimen at the time of collection. It would be impossible for the donor to substitute the specimen. The collector will examine the hair when collecting the specimen.

Issue 4: The only "dye test" in hair testing has been performed by one laboratory corporation (i.e., Psychemedics Corporation). The test was used as part of the "wash kinetics" procedure to detect porous hair. It does not help in assessing the specimen validity.

Issue 5: It is not possible for the testing facility to evaluate the split specimen (sample B) because the sealed B envelope is not opened.

Issue 6: A donor may have a mixture of colors (e.g., gray, dark, streaked, dyed). A difference in A and B specimens may not constitute an "abnormal physical characteristic."

6. Subject: Specimen Collection Procedures

Issue 1: The proposed Guidelines require a minimum amount of 100 mg for a hair specimen (50 mg each for A and B). This does not appear sufficient, given the amounts routinely used for hair testing: 12-15 mg for initial tests, 15-20 mg for each

confirmation test, and 20 mg for archive from Sample A. The Guidelines should be revised to require 150 mg head hair (i.e., with approximately 75 mg for specimens A and B).

Issue 2: Some instructions in the proposed Guidelines for hair specimen collection are unclear (e.g., placement of the hair specimen in the foil packet, use of separate tamper-proof envelopes for the A and B specimens).

Issue 3: Some terminology in the proposed Guidelines is not consistent with that currently used in the industry. For example, the term "specimen" should be used instead of "sample" and the term "container" instead of "tube" for oral fluid specimens.

7. Subject: Specific Gravity Testing

Discussion: It appears that the program's intent for requiring a 4-decimal place refractometer is to ensure that specimens reported as '"substituted" are able to withstand legal challenge. The refractometers currently in use in laboratories (i.e., 3-decimal place) are capable of providing accurate readings to report a specific gravity result in the "dilute" or acceptable ranges.

Issue 1: An IITF will not be allowed to report "substituted" or "invalid" specimens; these specimens will be forwarded to an HHS-certified laboratory. As written, requiring an IITF to perform specific gravity testing using a 4-decimal place refractometer seems an undue burden.

Issue 2: Laboratories also should be allowed to perform an initial specific gravity test using a 3-decimal place refractometer and be required to test the specimens with results < 1.003 or > 1.019 using a 4-decimal place refractometer.

To address both issues above, it is recommended that specific gravity testing be reflexed as follows:

> To address specimens that may be dilute with an initial creatinine test result greater than or equal to 2.0 mg/dL and less than 20.0 mg/dL, the initial specific gravity test may be performed using a 3-decimal place refractometer.

To address specimens that may be invalid with an initial creatinine test result greater than or equal to 2.0 mg/dL and less than 20 mg/dL and an initial specific gravity result less than 1.003 using a 3-decimal place refractometer, an HHS-certified laboratory would be required to perform specific gravity tests on two separate aliquots using a 4-decimal place refractometer.

- To address specimens that may be substituted (or invalid) with an initial creatinine result less than 2.0 mg/dL, the initial and confirmatory specific gravity tests must be performed by an HHS-certified laboratory using a 4-decimal place refractometer.

8. Subject: Specimen Validity Test Validation

Discussion: The proposed Guidelines include validation requirements for initial and confirmatory drug tests by laboratories (Section 11) and IITFs (Section 13), but do not include any validation requirements for specimen validity tests in these testing facilities.

9. Subject: Initial Drug Test Validation

Discussion: The following recommendations for initial drug test assay validation are submitted in response to the HHS request for comments on this subject:

- Specify that the testing facility must document the performance of the test ***for at least 6*** concentrations between 0 and 150 percent of the cutoff concentration.

  Include a requirement to assess the potential for carryover from highly concentrated samples during the initial test assay validation (and delete this requirement from the section listing initial test batch QC requirements).

  Specify that the Guidelines requirement to verify performance of new lots prior to placement into service is referring to initial test *reagent* lots.

10. Subject: Confirmatory Drug Test Validation

Discussion: The following recommendations for confirmatory drug test assay validation are submitted in response to the HHS request for comments on this subject:

- Include a requirement to assess the potential for carryover from highly concentrated samples during confirmatory assay validation (and delete this requirement from the section listing confirmatory test QC requirements).
- Include a requirement for periodic reverification of linear range, LOD, LOQ, and potential for interfering substances for confirmatory test assays (and delete this requirement from the section listing confirmatory test QC requirements).

11. Subject: Confirmatory Drug Test Quality Control

Discussion: The proposed Guidelines are worded to require single-point calibration. There is no technical justification for prohibiting laboratories from having multi-point calibration.

12. Subject: Defining "Invalid Result" as a "Non-Negative Result"

Discussion: The revised HHS Guidelines to go into effect on November 1, 2004 define an "invalid" result as a non-negative result. This definition should be maintained in this version of the Guidelines. Laboratories must continue to report "invalid result" in conjunction with any other non-negative result(s) for a specimen.

13. Subject: Drug Test Analytes

Discussion: Drugs/drug classes are not consistently and accurately described in the Guidelines for each specimen type. For example, the Initial Test Cutoff Concentration Table for hair specimens lists "cocaine metabolites" instead of "cocaine and metabolites." The Confirmatory Test Cutoff Concentration Table for oral fluid lists "THC Parent Drug," although there is no marijuana confirmatory test for oral fluid specimens (i.e., when an oral fluid specimen is presumptive positive for THC, the confirmatory test

for marijuana metabolite will be on the associated urine specimen).

14. Subject: Decision Points for Adulterant Tests

Discussion: For adulterant tests without a program-specified cutoff, testing facilities should use the limit of quantitation (LOQ) rather than the limit of detection (LOD) as the decision point. The LOQ value ensures that the adulterant has been both appropriately identified and quantified.

15. Subject: Tests to be Performed by a Laboratory

Discussion: The proposed Guidelines require a laboratory to perform only the confirmatory tests needed to confirm the presumptive non-negative results for specimens submitted by an IITF. A laboratory should test such specimens using the same tests used for primary specimens that have not been tested (i.e., initial drug and validity tests, reflexed to confirmatory drug and validity tests as needed). This would allow a single facility (the laboratory) to perform the tests and maintain complete drug test records for specimens that they report (e.g., all data supporting a non-negative result). The records would be available for review at the time of certification by the CT/CS at the laboratory and also be available for review during NLCP inspections. The program has always required a single individual to certify results by reviewing all data and associated chain of custody documents for a specimen. It is recommended that HHS maintain this policy, to ensure the scientific validity and forensic defensibility of specimen drug tests.

16. Subject: Oral Fluid Specimens and Associated Urine Specimens

Discussion: The proposed Guidelines require that a urine specimen be collected when an oral fluid specimen is collected. For oral fluid specimens testing positive for cannabinoids, the proposed Guidelines instruct POCT testers and IITFs to send only the urine specimen to an HHS-certified laboratory (i.e., and *not* send the oral fluid

specimen). For oral fluid specimens with any other non-negative result, the POCT testers and IITFs are instructed to send only the oral fluid specimen to the laboratory.

Issue 1: An HHS-certified laboratory must test specimens received from a POCT tester "in the same manner as a specimen that had not been previously tested." Therefore, the POCT tester must always send the non-negative oral fluid specimen and associated urine specimen to the laboratory, so the laboratory can perform initial testing of the oral fluid specimen.

Issue 2: As described in Subject 15 "Tests to be Performed by a Laboratory," we believe that laboratories should perform initial tests for specimens received from IITFs (i.e., not just confirmatory testing). Therefore, as recommended in Issue 1 above for the POCT tester, the IITF should always send the non-negative oral fluid specimen and associated urine specimen to the laboratory, so the laboratory can perform initial testing of the oral fluid specimen.

Issue 3: The Guidelines should clearly and consistently indicate that confirmatory THC testing is NOT performed for oral fluid specimens based on a positive cannabinoids initial test. When an oral fluid specimen is presumptive positive for THC, an HHS-certified laboratory must test the associated urine specimen.

Issue 4: There is no guidance on handling/disposal of the remaining oral fluid or urine specimen. (This would not be an issue if the above changes were made.)

Issue 5: There is no guidance for specimens with multiple non-negative results that include cannabinoids. (This would not be an issue if the above changes were made.)

17. Subject: Tests to be Performed by a POCT Tester

Discussion: The proposed Guidelines do not state what specimen validity tests are to be performed on specimens at a POCT site. This is addressed for laboratories and IITFs (Items 3.8 to 3.11), but is not addressed for POCT testers. POCT testers should test each urine specimen for creatinine, pH, and oxidizing adulterants.

18. Subject: Tests to be Performed by an IITF

Discussion: As written, the proposed Guidelines indicate that HHS-certified IITFs test every primary specimen using the same initial drug and validity tests that would be used in an HHS-certified laboratory. This is true for all tests except pH tests. For pH testing, the program allows laboratories to perform a "screening" test for pH prior to the initial test. A screening test is defined as a pH paper test, dipstick test, or a colorimetric pH test that has a narrow dynamic range and does not support the program cutoffs for adulteration. Such tests can be used to determine whether an initial pH test is required (i.e., they can identify specimens in the acceptable range of 4.5 to 9.0). A screening test would be sufficient for an IITF, which must send all presumptive invalid or adulterated specimens to an HHS-certified laboratory.

Issue 1: An IITF should be allowed the following pH testing options:

1. to perform the pH screening test only,
2. to perform the pH screening test and to perform an initial pH test using a pH meter for those specimens with an unacceptable pH screening test result, or
3. to perform the pH initial test using a pH meter on all specimens.

Issue 2: PT scoring criteria for pH should be less stringent for an IITF than for a laboratory. It is sufficient for IITFs to correctly identify the qualitative pH and specific gravity results of PT samples (i.e., the same scoring requirements as qualitative validity tests.)

Issue 3: The Guidelines contain some references to IITF reports of "invalid result." IITFs are not allowed to report specimens as invalid. The Guidelines should be reviewed and revised for consistency.

19. Subject: POCT

Discussion: A number of significant changes are suggested to the proposed Guidelines section on POCT. These changes would carry the principles previously established in the NLCP for urine drug testing into the POCT arena and allow for realistic, cost-effective interaction and documentation among the various components

of the process.

Issue 1: SAMHSA proposes to conduct all evaluations of POCT devices to determine if they meet the requirements in Subpart L. The proposed process places an undue administrative/regulatory burden on the Government to have a device approved. This evaluation process would require at least 500 POCT devices. The receipt, inventory, storage and evaluation of these devices by the Secretary seems a monumental task. The POCT device manufacturer should be required to validate a POCT device lot in the same manner that an HHS-certified laboratory or IITF is to validate an initial drug test (described in Section 11.13 and required for IITFs in Section 13.5), documenting the same performance characteristics. The validation documentation would be submitted with the POCT device application.

Issue 2: After the application for a device lot has been reviewed and accepted, the POCT manufacturer should receive PT samples in a program analogous to that for an applicant laboratory or IITF. It is suggested that the question about criteria for HHS evaluation of a POCT device be revised to address the criteria to be used to evaluate performance in the PT cycles analyzed by the device manufacturer. The wording for the question should be similar to those addressing initial oral fluid and urine PT cycles for laboratories and IITFs (Sections 9.7 and 9.9).

Issue 3: The Guidelines state that, if requirements are met, a device will be "certified" for use and placed on the SAMHSA list. Using the word "certified" implies a standard of performance to the device and not the process (i.e., the device as utilized by a trained tester). Each manufactured *lot* of a device should be "approved" for use by a properly trained individual. This would generate a SAMHSA List of Conforming POCT Devices.

Issue 4: To allow the Secretary to test devices when a problem arises with the device, it is recommended that the manufacturer hold in reserve 500 POCT devices of the approved lot number for future submission.

Issue 5: The proposed processes for a device to continue on the SAMHSA-approved list (i.e., requiring the manufacturer to submit a description of any design changes or alterations for an approved device to the Secretary and annual monitoring of device

performance) appear impractical and unnecessary. Other sections of the proposed Guidelines already include criteria for device failure and subsequent program action which includes removal from the approved list. If a device lot number is removed from the list, the manufacturer must repeat the application process.

Issue 6: Because expected expiration dates range from 12 to 18 months, requirements for annual monitoring of device performance do not appear necessary. Other sections of the Guidelines provide for ongoing monitoring of approved device lot performance. It is anticipated that a manufacturer would complete the process for the next lot number before the currently approved lot number expires or that a manufacturer would have more than one lot number listed.

Issue 7: The proposed Guidelines delegate oversight responsibility to the Federal agencies for POCT performed in their workplace programs. Therefore, the Agency should assume responsibility for POCT quality assurance. This should include a PT program to verify the continued competency of *the individual testers*. POCT sites are not certified and testing may not even be at a permanent site. Individual testers are required to have documented training and these records can be used by the Federal Agency to identify the individual testers for the PT program.

Issue 8: Some of the proposed POCT PT sample concentrations are not appropriate to challenge POCT cutoffs/decision points. The concentrations should be adjusted to challenge the cutoffs/decision points while avoiding overlap across the cutoff/decision points. Also, POCTs will not be used for specific gravity tests, so there is no need for specific gravity PT samples. (Also see Subject 24, Oral Fluid Validity Testing: It is recommended that the criterion for an oral fluid PT sample to contain IgG be deleted. It is unclear if a POCT device would be capable of performing this test.)

Issue 9: The proposed Guidelines should allow the Secretary to inspect a POCT site. As written, the proposed Guidelines require the Federal Agencies to inspect the POCT sites and allow the Secretary "to conduct a semiannual inspection of each Federal agency that uses a POCT." However, the proposed Guidelines do not state that HHS may conduct an on-site inspection of a POCT site.

Issue 10: Because a POCT tester will perform the first test on a specimen (in effect, mimicking the laboratory part of initial testing), it seems prudent to have the POCT tester analyze a PT sample set and demonstrate their proficiency before becoming initially approved to use a particular POCT device.

Issue 11: The Guidelines should clearly state that presumptive non-negative POCT specimens and the CCFs are sent to a laboratory under chain of custody.

Issue 12: The Guidelines should clearly state that each tester is to test QC on each device they use, should give the same guidance for validity POCTs, and should require documentation of all POCT QC results.

Issue 13: The proposed Guidelines require a POCT tester to send failed QC samples to an HHS-certified laboratory. This serves no purpose and is not cost-effective. The Federal Agency SOP should describe investigative/corrective actions to be taken in the event of a failed QC sample. The Guidelines should instruct the POCT tester **not** to test donor specimens when a QC sample fails, and to send specimens to a certified laboratory for testing.

Issue 14: The Guidelines should clearly describe the reporting options for a POCT tester.

Issue 15: The statistical summary report from the Federal Agency should have items appropriate for POCT testing and provide the same information as the statistical summary reports from HHS-certified laboratories and IITFs. A requirement should be added to report the number of negative specimens sent for the QA program (i.e., 10 percent of negative specimens). These can then be audited. The requirement to enumerate the QC samples should be deleted. This information will be part of Section 12.11(a)(4) that is available to the Secretary at the semiannual inspections of the Federal agency. **Note:** Requirements for the IITF statistical summary report should be revised to be similar.

20. IITF PT requirements

Discussion: IITFs should be required to meet the same PT requirements as

laboratories for initial drug test challenges. The Guidelines sections for applicant and certified IITF PT scoring should be revised to have the same criteria as for laboratories.

21. Subject: pH Testing Requirements

Discussion: The revised Guidelines require the refractometer to print a hardcopy report or to be interfaced with a LIMS/computer. The same requirements should be in place for pH meters. The same forensic considerations apply. There are pH meters currently available with this technology.

22. Subject: Oral Fluid and Sweat Methamphetamine Positive Specimens

Discussion: The Guidelines state a concentration for amphetamine to report methamphetamine as positive in hair specimens and urine specimens. An amphetamine quantitative value also should be specified for oral fluid and for sweat, rather than stating that amphetamine must be present above the LOD (an undefined value) to report methamphetamine as positive.

Subject: Sweat Testing

Issue 1: The proposed Guidelines should be revised to accurately and consistently describe the analytes for sweat testing (e.g., marijuana analytes listed in the Initial Test Cutoff Concentration table and the Confirmatory Test Cutoff Concentration table).

Issue 2: There are currently no data to support testing lactic acid in sweat as a validity test. If scientific information is obtained that supports keeping the requirement for lactic acid testing in the Guidelines, the following must be addressed:

- There is a requirement to determine the lactic acid concentration on every sweat patch sample. However, there are no defined limits for this analyte to evaluate if the specimen is substituted or invalid (i.e., there are no definitions for substituted or invalid sweat specimens as there are for oral fluid and urine specimens).
- The Guidelines do not have requirements for testing, reporting, or scoring PT samples containing lactic acid. This is inconsistent with sections describing PT

requirements for urine.

Lactic acid test requirements must be clearly defined. It is unclear whether there are lactic acid tests that meet the Program criteria for initial and confirmatory tests.

23. Subject: Oral Fluid Validity Testing

Discussion: The proposed Guidelines require testing of Immunoglobulin G (IgG) in oral fluid to determine specimen validity. It is unclear whether there are data to support this as a validity test. If scientific information is obtained that supports keeping the requirement for IgG testing in the Guidelines, the following must be addressed:

- The Guidelines define a "substituted" oral fluid specimen as one with an IgG concentration < 0.10 mcg/mL. However, the Guidelines do not require both initial and confirmatory IgG tests. This is inconsistent with criteria for reporting a urine specimen as substituted (Section 3.17).
- There are no Guidelines requirements for testing, reporting, and scoring PT samples containing IgG. This is inconsistent with sections describing PT requirements for urine.
- IgG testing requirements must be clearly defined. It is unclear whether there are IgG tests that meet the Program criteria for initial and confirmatory tests.
- The proposed Guidelines section describing POCT lists IgG as a POCT analyte. It is unclear if a POCT device for oral fluids will be able to test for IgG. Also, the oral fluid specimen collection will be observed; there is no need to perform specimen validity testing. It is recommended that this be deleted as a POCT analyte.